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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/838,486	04/07/97	BAEKKESKOV S	02307U-3122

HM12/1014
TOWNSEND AND TOWNSEND AND CREW
TWO EMBARCADERO CENTER 8TH FLOOR
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EXAMINER	
TUNG, M	
ART UNIT	**PAPER NUMBER**
1644	14

DATE MAILED: 10/14/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/838,486	Baekkeskov
Examiner	**Group Art Unit**
Mary B. Tung	1644

☒ Responsive to communication(s) filed on *Jul 28, 1999*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *31, 34, 35, 38-42, and 49-59* is/are pending in the application.

Of the above, claim(s) *38-42* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *31, 34, 35, and 49-59* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Serial No. 08/838,486
Art Unit 1644

DETAILED ACTION

1. Claims 1-30 and 43-48 were cancelled in the preliminary amendment filed April 7, 1997.

2. Claims 32, 33, 36 and 37 have been cancelled in the amendment filed Nov. 2, 1998 Paper No. 9).

3. Non-elected claims 38-42 were withdrawn from consideration by the Examiner in the paper mailed April 28, 1998 (Paper No. 6).

4. Claims 49-57 were added in the amendment filed Nov. 2, 1998, Paper No. 9.

5. Claims 58 and 59 were added in the amendment filed 7/28/99, Paper No. 13.

6. Claims 31, 34, 35, 38-42, 49-59 are pending in this application.

In view of the amendment filed 7/28/99, the following rejections remain:

Claim Rejections - 35 U.S.C. § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Applicant's arguments filed in Paper No. 13 have been fully considered but they are not persuasive.

9. Claims 31, 34 and 35 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the same reasons set forth in the office action mailed 1/22/99, Paper No. 11.

10. The Applicants argue that there is "inconsistency between the maintenance of the rejection in the present application, and the issuance or indication of allowability of substantially similar claims in two other patent filings having priority dates approximately contemporaneous with that of the present application." Applicants' assertion that the instant claims are allowable because similar claims have issued or

been allowed in other cases is moot because the prosecution of each case is unique to the facts of each case. The Examiner also notes that the claims of the '937 patent by Atkinson, et al. are not co-extensive in scope.

11. The Applicants have not provided evidence to overcome the facts presented by the Examiner in previous actions by Tisch, et al. (X) teaches (page 437, col. 1) that the effectiveness of this therapy hinges on several factor: one is whether the therapy can be used to treat an ongoing autoimmune response or whether it is useful only in preventing the disease, and the Applicants have failed to disclose a method of treatment using GAD that would actually prevent the onset of IDDM, or by by Benjamani and Leskowitz ((U2) page 256, paragraph 2) that "tolerance *can* be induced by opposite extremes of dosage., or by Tian, et al. (U3) that teach that they could induce an antigen-specific anti-inflammatory Th2 response and inhibit disease progression in NOD mice, Tian describes a 65kD GAD antigen, whereas the Applicants have disclosed a 64kD GAD antigen, disclosed by the Applicants on page 4 as being different with respect to hydrophobicity, solubility and isoelectric point (see lines 20-31) and also teach that treatment of NOD mice and humans at risk for IDDM may differ due to the "complexity of the autoreactive T-cell population and the genetic diversity of MHCs within the [human] patient population." The Applicants have not taught how to use their invention to deal with the high degree of specificity required for the process of clonal deletion/anergy may be limiting when dealing with diseases such as MS, IDDM and rheumatoid arthritis, in which there are responses to several antigens.

12. The issue of pharmacological evidence have been discussed in Paper No. 11.

13. Issues concerning 35 U.S.C. 101 have been discussed in Paper No. 11 and do not apply in the instant application since the rejection was not made.

14. Additionally, the Applicants arguments concerning Lernmark (W) are not persuasive since they are mere allegations without a showing of factual evidence. Lernmark teaches that "Further experiments also extended to the spontaneously diabetic BB rat are warranted to determine the mechanism of protection, especially *as other investigators have not found the published procedures to be easily reproducible.*" ((W), see page 274, col. 2, paragraph 1, in particular). Given the lack of reproducibility tin the art taught by Lernmark, the lack of working examples in the instant application would not allow one of skill in the art to practice the invention as claimed.

15. The Applicants have supplied a copy of a reference by Elliott, et al. *(Diabetes, 43:1494-1499, 1994)* as evidence. Elliot, et al. teach that the 65 kDa isoform of GAD "is implicated in autoimmune diabetes", (see the abstract) and the treatment of NOD mice with the 67kDa isoform of GAD. The use of the NOD mouse model is discussed,

supra, and the 67 kDa isoform is not claimed in the instant application. The Applicants have additionally provided a reference by Petersen, et al *(Diabetes, 44:1478-1484, 1994)*, which teaches the use of the 65 kDa GAD in neonatal NOD mice. Petersen also teaches that "Since we have demonstrated that mouse islets contain only very little GAD, the reported T-cell reactivity against mouse islets proteins will most likely have to be explained by other autoantigens, Taken together, these observations show that although GAD autoimmunity is necessary, it is not sufficient for the development of NOD mouse diabetes." (see page 1482, col. 2). Peterson, et al. additionally teach that GAD_{65} could prevent spontaneous diabetes in NOD mice, but that autoantibodies to GAD were detected in injected mice. This seemingly contradictory data is explained by Petersen by saying that the "autoantigenic properties of GAD in NOD mice islets are not well understood." (see page 1482, col. 2, last paragraph). A reference by Bu, et al. *(Proc. Natl. Acad. Sci. USA 89:2115-2119, 1992)* was also supplied by the Applicants. Bu et al. teach the isolation and sequencing of cDNAs encoding GAD_{65} and teach that GAD "is the earliest known autoantigen during the development of IDDM" (see page 2119), no data was taught of a method of treatment using GAD to prevent the onset of IDDM. Apparently, the state of the art at the time the invention was made was uncertain and the Applicants' arguments are unpersuasive.

16. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification, it would take undue trial and errors to practice the claimed invention and the rejection stands.

17. Claims 34, 49-53 and *new claim 58* stand rejected under 35 U.S.C. 112, first paragraph, for the same reasons set forth in Paper No. 11 as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, unpredictability in the art, the amount of experimentation required, the lack of working examples, and the amount of direction or guidance presented.

18. The issues regarding the rejection under 35 U.S.C. 112, first paragraph as pertaining to claims 34 and 49-53 are the same as those pertaining to claims 31 and 35 and are discussed, *supra.*

Claim Rejections - 35 U.S.C. § 102

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --
(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the Applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the Applicant for patent.

20. Claim 31 stands rejected under 35 U.S.C. 102(e) as being anticipated by Atkinson (US Patent No. 5,762,937), for the same reasons set forth in the action of Paper No. 11.

21. A method for inhibiting the development of IDDM comprising the administration to a patient GAD is taught in col. 4, lines 40-48 and col. 25 line 53 and bridging over to col. 26, line 14. The administration of a therapeutically-effective dosage is inherent in the successful treatment of any disease. Therefore, the reference teachings anticipate the claimed invention. The rejection as cited in Paper No. 11 was inadvertently cited as 102(a). The Examiner thanks the Applicants for correction of this typographical error.

Claim Rejections - 35 U.S.C. § 103

22. The following is a quotation of *35 U.S.C. § 103* which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
Subject matter developed by another person, which qualifies as prior art only under *subsection (f) or (g)* of *section 102* of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

23. It is acknowledged that the Applicants have stated in Paper No. 13 that the subject matter of all claims was commonly owned by the University of California and Yale University.

24. Claims 35 and 54-57 stand rejected under 35 U.S.C. 103(a) as being obvious over Chang and Gottlieb (AX).

25. The Applicants argue that it would not be obvious to combine GAD with a carrier for humans because the purpose of Chang and Gottlieb (AX) is to generate monoclonal antibodies, which involve the probable euthanasia of the animal. While the practice of routinely euthanising a valuable antibody-producing animal is debatable, one of ordinary skill in the art at the time the invention was made would have been motivated to provide a pharmaceutically-acceptable carrier for humans in light of the teaching by Chang and Gottlieb of a pharmaceutically-acceptable carrier for use in rats, especially

since pharmaceutical carriers are well known to one of ordinary skill in the art for use in humans. The limitations of the claim only requires that the composition be pharmaceutically acceptable in humans. The composition of a buffer, such as PBS, is inherent in the teaching absent evidence to the contrary. Claims *54-56* are included because a product is a product, regardless of its source. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

26. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

The following new grounds of rejection is necessitated by amendment:

27. Claims 58 and 59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no support in the specification or claims as originally filed for a human GAD65. Only rat GAD65 is disclosed. **This is a new matter rejection.**

Conclusion

28. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

29. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

30. Papers related to this application may be submitted to Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published

in the Official Gazette, 1096 OG 30 (November 15, 1989). THE CM1 FAX CENTER TELEPHONE NUMBER IS (703) 305-3014 or (703) 308-4242.

31. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Mary Tung whose telephone number is (703)308-9344. The Examiner can normally be reached Tuesday through Friday from 8:30 am to 5:30 pm, and on alternating Mondays. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1640 receptionist whose telephone number is (703) 308-0196.

Mary B Tung

October 12, 1999
Mary B. Tung, Ph.D.
Patent Examiner
Group 1640

David A. Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644